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## Remarks

Claims 1-91 are pending in the subject application. Applicants acknowledge that claims 13-51 have been withdrawn from further consideration as being drawn to a non-elected invention. By this Amendment, Applicants have amended claim 1 and canceled claims 12, 66, 79-86, 88, and 89. Support for the amendments can be found throughout the subject specification and in the claims as originally filed (see, for example, original claim 12, paragraphs 12, 34, 50, 106, 232, 239, 248, 249, 252, 279, and 283 of the substitute specification filed February 19, 2002). Entry and consideration of the amendments presented herein is respectfully requested. Accordingly, claims 1-11, 52-65, 67-78, 87, and 91 are currently before the Examiner. Favorable consideration of the pending claims is respectfully requested.

In response to the Advisory Action dated October 15, 2004, Applicants respectfully submit that the "metal bar" limitation of amended claim (i.e., claim 1) not only finds support at the paragraphs indicated in the previous response, but also at previously pending claim 12 of the application which explicitly contained the limitation added to claim 1. Additionally, paragraph 12 last sentence clearly provides support for the amendment made to claim 1. A copy of the relevant portions of the substitute specification, including page 1 providing an indication that the substitute specification was "OK to Enter" is attached for the Examiner's convenience. Accordingly, reconsideration of the denial of entry of the previously filed amendment is respectfully requested.

Applicants wish to, again, thank the Examiner for the courtesy of the interview held September 8, 2004. Applicants concur with the Interview Summary (IS) indicating the substance of the discussions held with the undersigned. As indicated in the IS, discussions relating to support for various previously presented claim amendments were held as were discussions related to the prior art of record and various limitations of the claims which Applicants contend are not rendered obvious by the combination of references of record in this matter.

With respect to the issue of the substitute specification, a second review of the record and the electronic file wrapper of the application indicates that a substitute specification was filed on February 19, 2002 by previous counsel (entry of which was indicated in the Office Action of June 19, 2002). The images of this substitute specification reviewed by the undersigned contain what appear to be hole punches well above the text of the specification. Accordingly, it is not believed

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that another substitute specification is required and withdrawal of this requirement in the next Office Action is respectfully requested. Applicants also request the electronic records of the Patent Office be updated to reflect the new title presented in the last response. A review of the Patent Office electronic records indicates the new title is not yet reflected therein.

Applicants note that the claims have been objected to on the basis that several newly presented dependent claims are separated from the independent claim from which they depend by another independent claim. Applicants have attended to this issue by cancellation of the intervening independent claim (and claims dependent therefrom) and respectfully request withdrawal of the objection.

The Office Action has rejected claims 73, 74, 77, 78, 80, 81, and 84-91 on the basis that the claims are not supported by the as-filed specification and that the claims are new matter to the subject application. Applicants respectfully submit that the claims are supported by the as-filed application and support can be found at the following locations in the substitute specification filed February 19, 2002.

Claim(s)	Page(s), Paragraph
73, 80	70, 248
74, 81	72, 252
75, 82	62, 232
76, 83	64-65, 239
77, 84	77, 279
78, 85	78, 283
86, 87	70-71, 249
88, 89, 90, 91	28, 106

Accordingly, it is respectfully submitted that the claimed invention finds support for the various temperatures between which the temperature regulated zone(s) cycle and withdrawal of the rejection is respectfully requested.

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Claims 1-12 and 52-91 have been rejected over Kopp et al. in view of Poser et al. and United States Patent No. 5,587,128 (Wilding et al.). Applicants respectfully traverse. It is respectfully submitted that the combination of Kopp et al., Poser et al., and Wilding et al. fail to render the claimed invention obvious. Principally, the combination of references fails to teach or suggest a device comprising: a microfluidic substrate comprising at least one sample pathway for sample flow; and said microfluidic substrate further comprising at least one temperature regulated zone that cycles between at least two different and predetermined temperatures, said at least one temperature regulated zone being adapted to bring at least a portion of said sample pathway to said at least two temperatures while a sample is unidirectionally flowing along said at least a portion of said sample pathway and said at least one temperature regulated zone comprising a metal bar in fluid communication with a plurality of water sources containing water at said at least two temperatures, said metal bar being in thermal communication with said at least a portion of said sample pathway and wherein a sample is cycled between said at least two different and predetermined temperatures while in said at least one temperature regulated zone. In view of the failure of the references to teach a metal bar in fluid communication with a plurality of water sources, it is respectfully submitted that the combination of references fails to render the claimed invention prima facie obvious and withdrawal of the rejection is respectfully requested.

It should be understood that the amendments presented herein have been made <u>solely</u> to expedite prosecution of the subject application to completion and should not be construed as an indication of Applicants' agreement with or acquiescence in the Examiner's position. Applicants expressly reserve the right to pursue the invention(s) disclosed in the subject application, including any subject matter canceled or not pursued during prosecution of the subject application, in a related application.

In view of the foregoing remarks and amendments to the claims, Applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

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Applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,

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Attachments: Pages 1, 3, and 4 of the substitute specification